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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,473	05/31/2000	BARBARA BOTTAZZI	2801-18	9420

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NIXON & VANDERHYE
1100 NORTH GLEBE ROAD
8TH FLOOR
ARLINGTON, VA 22201-4714

EXAMINER

JAMROZ, MARGARET E

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 12/20/2001

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/555,473

Applicant(s)

BOTTAZZI ET AL.

Examiner

Margaret E Jamroz

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1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 12-16 is/are pending in the application.
- 4a) Of the above claim(s) 6-8 and 12-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

1. The Art Unit location and the examiner of your application in the PTO have changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Megan Jamroz, Art Unit 1644, Technology Center 1600.

2. Applicant's election with traverse of Group I (claims 1-5) in Paper No. 13 is acknowledged. The traversal is on the ground(s) that examination of the subject matter would not be an undue burden. This is not found persuasive because of the different classification searches and recognized divergent subject matter of the Groups.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's request to rejoin newly added claims 13-16 with Group I (claims 1-5) is noted, however, as the allowability of Group I has not been decided, it is inappropriate to discuss rejoinder at this time. See MPEP 821.

Claims 6-8 and 12-16 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a non-elected invention.

Claims 1-5 are under consideration in the instant application.

3. Applicant's IDS, filed May 31, 2000 is acknowledged.

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

5. Formal drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

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6. The disclosure is objected to because of the following informalities: a description of Figure 1 is missing from the Brief Description of the Drawings.

Appropriate correction is required.

7. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) Title of the Invention.
- (b) Cross-References to Related Applications.
- (c) Statement Regarding Federally Sponsored Research or Development.
- (d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
- (e) Background of the Invention.
 - 1. Field of the Invention.
 - 2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (f) Brief Summary of the Invention.
- (g) Brief Description of the Several Views of the Drawing(s).
- (h) Detailed Description of the Invention.
- (i) Claim or Claims (commencing on a separate sheet).
- (j) Abstract of the Disclosure (commencing on a separate sheet).
- (k) Drawings.
- (l) Sequence Listing (see 37 CFR 1.821-1.825).

8. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

9. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Italy on December 19, 1997. It is noted, however, that a certified copy of the RM97A000796 application as required by 35 U.S.C. 119(b) has not been received.

10. Claim 3 is objected to because of the following informalities: "FITX3" in line 2 should be "PTX3". Appropriate correction is required.

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11. Claim 3 is objected to because of the following informalities: "o" in line 2 should be "or". Appropriate correction is required.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a single disclosure of a human PTX3 protein (i.e. SEQ ID NO: 1) cloned into a murine mastocytoma cell line and injected into a mouse to show anti-tumor activity, does not reasonably provide enablement for a pharmaceutical composition containing the amino acid sequence of the **genus** protein, PTX3, and a pharmacologically acceptable excipient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make AND/OR use the invention commensurate in scope with these claims.

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated amino acid sequences having or encoding any PTX3 protein encompassed by the claimed invention other than "proteins set forth by SEQ ID NO: 1" would be expected to have greater differences in their activities.

It is known in the art that even single amino acid changes or differences in a proteins amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama et al. (PNAS, 1993. 90: 10056-10060) teach that the human glycosylation factor (GIF) protein differs from human macrophage

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migration inhibitory factor (MIF) by a single amino acid residue (see Figure 1 in particular). Yet, Mikayama et al. further teach that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF activity (see Abstract in particular).

Skolnick and Fetrow (Trends in Biotechnology, 2000. 18(1): 34-39) teach that determining the sequence of a nucleic acid molecule does not provide sufficient information to obtain the structure of a protein. Furthermore, the function of a protein cannot be determined simply by knowing the structure of a protein, as many proteins are multifunctional. Changes in nucleic acid sequences can, therefore, potentially result in changes in essential three-dimensional structures of the given protein, and consequently, its function.

Since the amino acid sequence of a polypeptide determines its structure and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality requires a knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification) and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain binding or functional aspects of PTX3 proteins, and finally, what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation.

In re Fisher, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since the amino acid sequence of a polypeptide determined its structural and functional properties, predictability of which fragments will retain functionality requires a knowledge of, and a guidance with regard to, which amino acids in the polypeptide's sequence contribute to its structure, and therefore, function. The problem of predicting which fragments or derivatives of a protein will retain functionality and which will not is complex and well outside the realm of routine experimentation. Because of the lack of sufficient guidance and predictability in determining which structures would lead to functional PTX3 proteins with the desired properties and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al, in The Protein Folding Problem and Tertiary Structure Prediction, 1994. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of proteins encompassed by the claimed invention.

Further, applicant has shown a single instance of anti-tumor activity by cloning human PTX3 into the murine mastocytoma P815 cell line which is then injected into mice as disclosed in the specification on page 9, line 3. However, applicant has not shown any working examples of a composition of human PTX3 and a pharmacologically acceptable excipient for the treatment of **any** bacteria, **any** fungi, **any** protozoa, or **any** tumor.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

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17. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a single species of human PTX3 protein (i.e. SEQ ID NO: 1) cloned into a murine mastocytoma cell line and injected into a mouse which exhibited anti-tumor activity.

There is insufficient written description to show that applicant was in possession of the claimed pharmaceutical composition containing the amino acid sequence of the long pentraxin PTX3, a genus protein, and a pharmacologically acceptable excipient. Applicant is also not in possession of every conceivable amino acid sequence comprising a PTX3 protein which could be used in a pharmaceutical composition. Disclosure of one species does not encompass every conceivable PTX3 and does not provide sufficient support for the entire genus. One of skill in the art would therefore conclude that the specification fails to disclose a representative number of species to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Alles et al. (Blood, 1994. 84(10): 3483-3493).

Alles et al. teach a composition comprising a naturally occurring human PTX3 from human peripheral blood mononuclear cells and a pharmacologically acceptable excipient (i.e. saline) injected subcutaneously into an animal (see entire document, the abstract and page 3485, column 1, paragraph continued from page 3484 regarding the production of antibodies to PTX3).

Applicant is notified that the uses of the composition in claims 4-5 are not given patentable weight since they do not contribute to the structure or function of the composition.

Therefore, the Alles et al. references anticipates the claimed invention.


20. No claim is allowed.

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21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Megan Jamroz, whose telephone number is (703) 308-8365. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Margaret (Megan) Jamroz, Ph.D.
Patent Examiner
Technology Center 1600
December 18, 2001


PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
12/20/01